

1

## BEFORE MEDICAL IMAGING

Knowledge of structure and function of the human body in health and disease limited to

external observation

studies of blood and urine

detailed post-mortem dissection



*Theatrum anatomicum in Leiden, copperplate engraving ~1615*

2

# NOVEMBER 8<sup>th</sup>, 1895: DISCOVERY OF X-RAYS



Wilhelm Röntgen



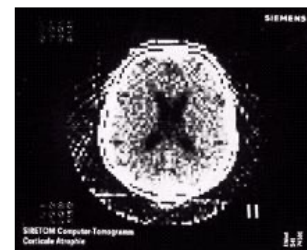
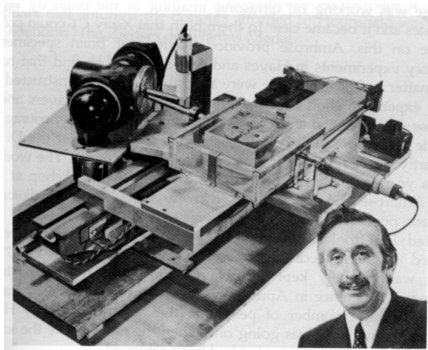
First image  
Dec 21<sup>st</sup>, 1895



First paper on X-rays,  
published Dec 28<sup>th</sup>, 1895

# 1971: COMPUTED TOMOGRAPHY (CT) SCANNER

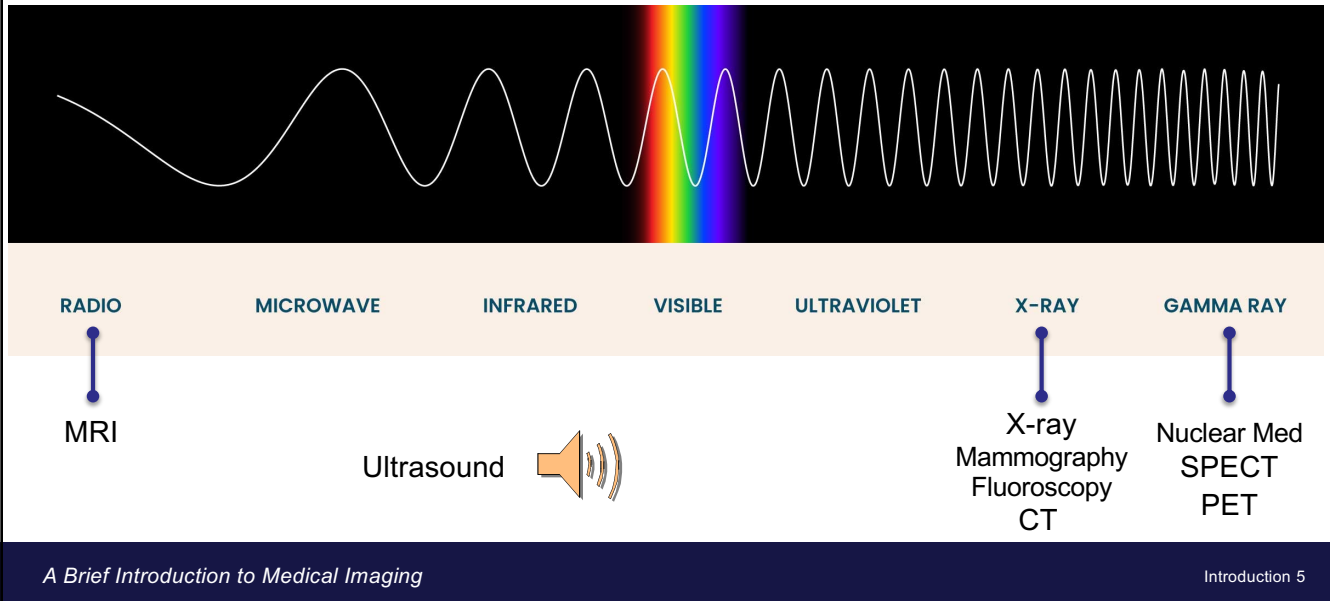
GODFREY HOUNSFIELD



Early CT scan  
~1975

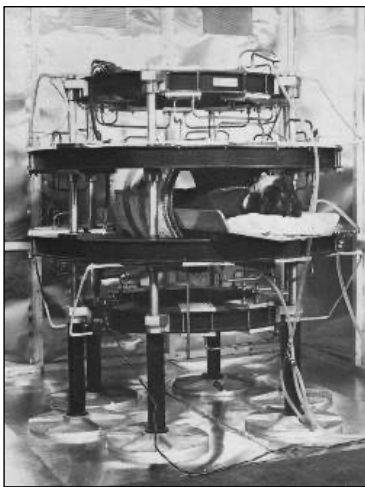
Other key contributors to tomography include  
Johann Radon, William Oldendorf and Allan Cormack

# RADIATION USED FOR IMAGING



5

# MEDICAL IMAGING: FROM PHYSICS TO SYSTEMS

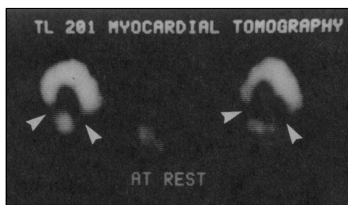
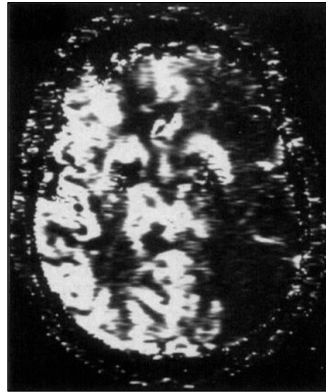
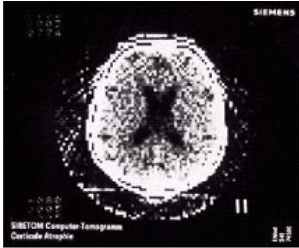


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Introduction 6

6

# MEDICAL IMAGING: EARLY IMAGES

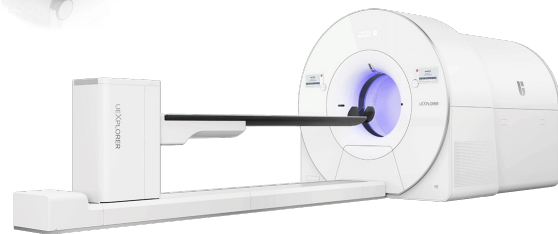


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Introduction 7

7

# MEDICAL IMAGING: ENGINEERING REVOLUTION

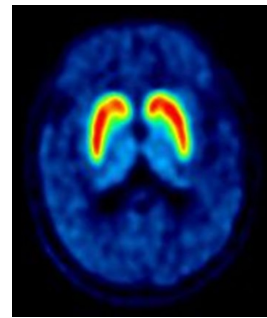
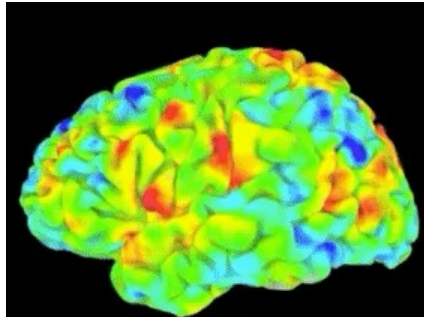
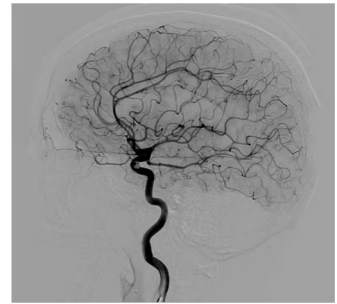
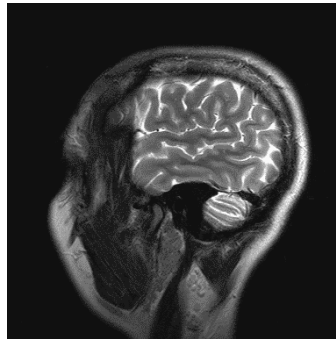


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Introduction 8

8

# MEDICAL IMAGING BRAIN

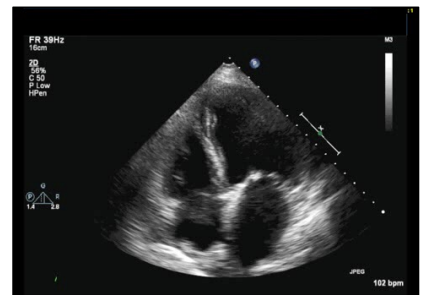
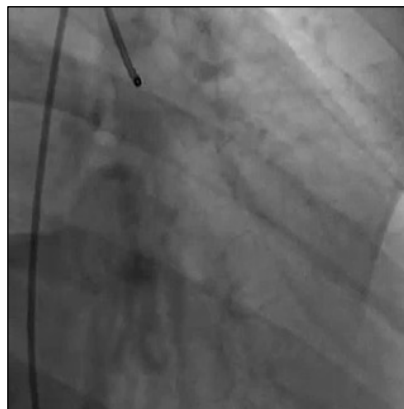
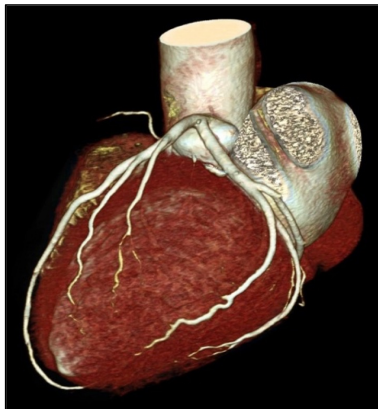


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Introduction 9

9

# MEDICAL IMAGING HEART

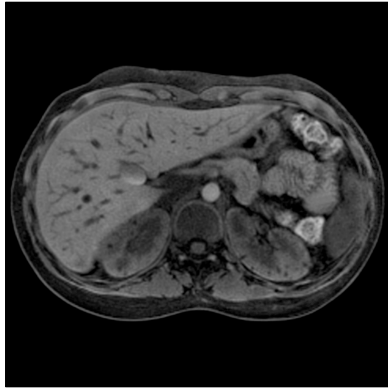


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Introduction 10

10

# MEDICAL IMAGING ACROSS THE BODY



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Introduction 11

11

## How Do Imaging Modalities Differ?

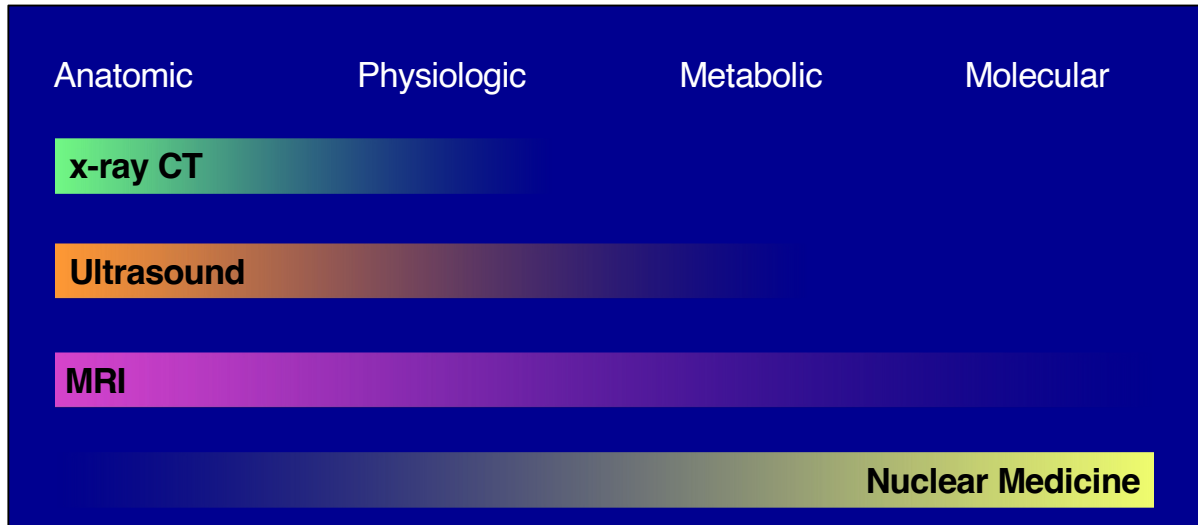
- What do they measure
- Spatial scale of measurement
- Temporal scale of measurement
- Sensitivity of measurement
- Field of view of measurement
- Cost of measurement
- Hazard/risk associated with measurement

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Introduction 12

12

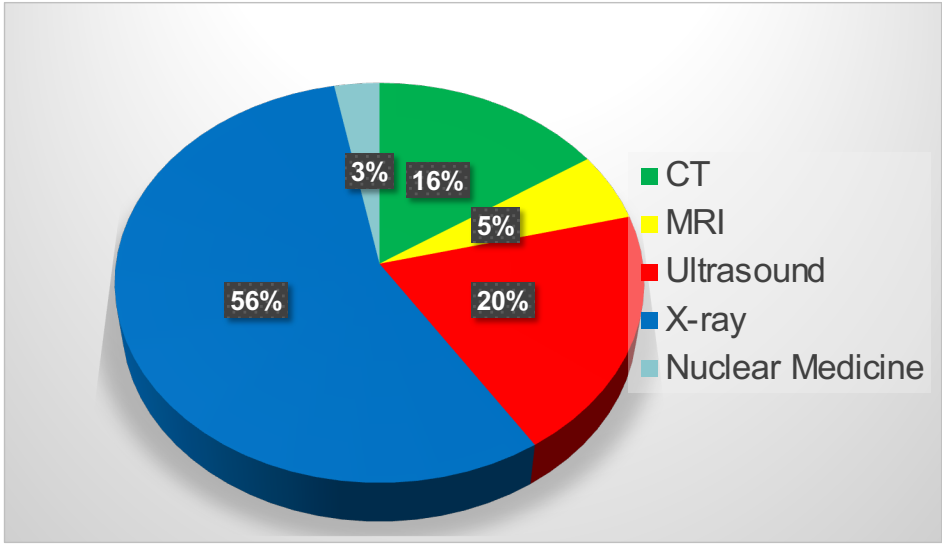
# Biomedical Imaging



## Impact

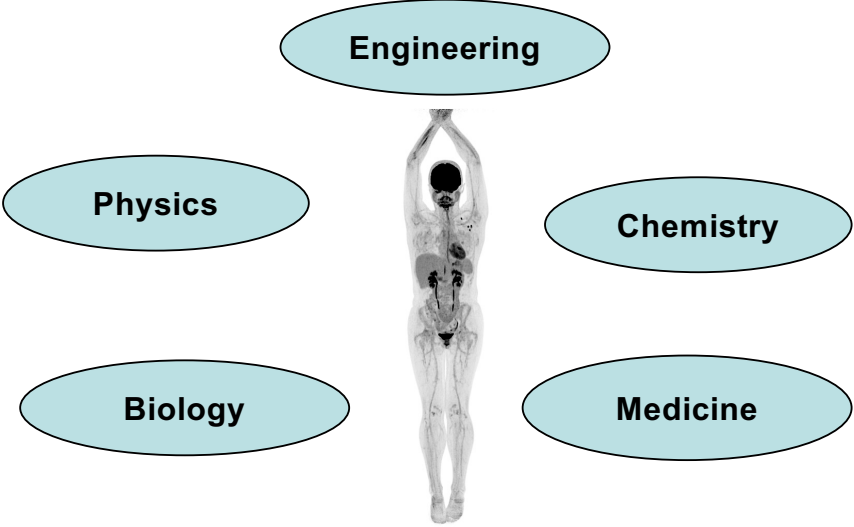
- Medical imaging plays a role in the assessment of virtually every injury and many forms of disease.
- ~ 400 million medical imaging procedures per year in the U.S.A.
- Medical imaging has improved diagnosis and saved many lives

# Utilization



Global market  
~\$25B (2017)

# Medical Imaging is a Multidisciplinary Field





## Careers in Biomedical Imaging

- Industry
  - Medical Imaging Companies
    - Siemens, GE, United Imaging, Philips etc...
  - Pharmaceutical/Biotech Companies
    - Genentech, Merck, Pfizer, Novartis etc...
  - Contract Research Organizations
    - Invicro, Imaging Endpoints, etc...
  - Detector companies
    - Hamamatsu, Broadcom,...
  - Software companies (AI!)
    - Mirada, Subtle Medical, Amira...

## Careers in Biomedical Imaging contd...

- Academia/Education
  - Research
  - Teaching
- Hospitals/Medicine
  - Radiology (Med School first!)
  - Medical physics/engineering
- Other...
  - Funding agencies
  - Patent Office
  - Scientific publishing/journals
  - Scientific consulting

## Societal Issues for Biomedical Imaging

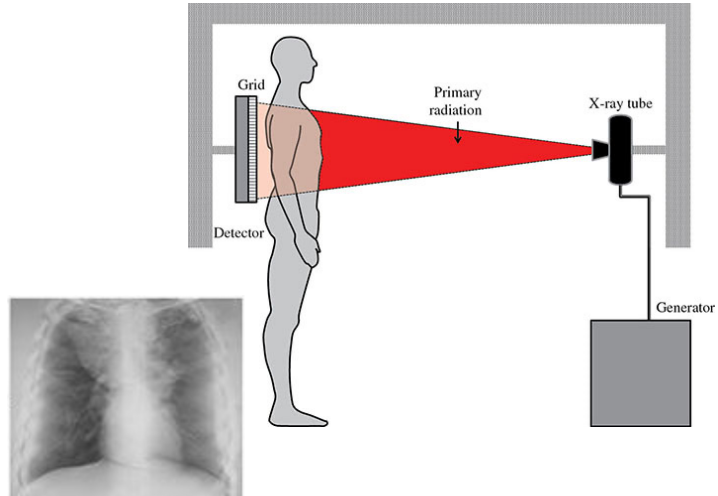
- \$\$\$ Cost
- Equitable access
- Radiation dose (where applicable)
- Total body screening – overdiagnosis/treatment?
- Diagnosis in absence of treatment

## X-Ray Imaging



# General Principles

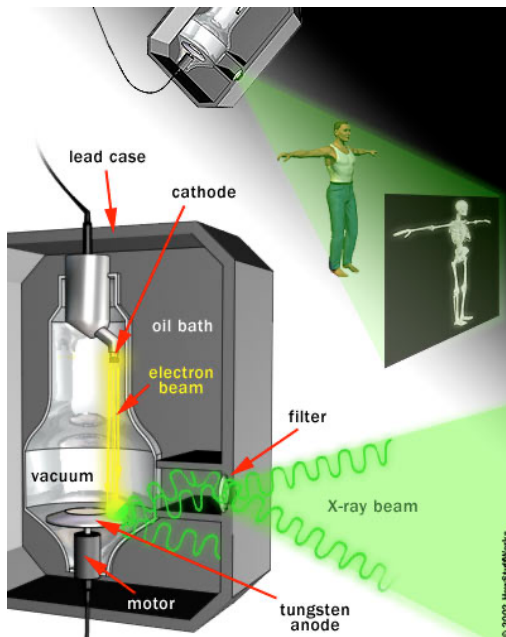
- Transmission-based technique
- X-rays pass through patient and detected by film or detector
- Contrast arises from differential attenuation of X-rays in body
- Planar radiography, image is a 2-D projection of tissues lying between x-ray source and detector



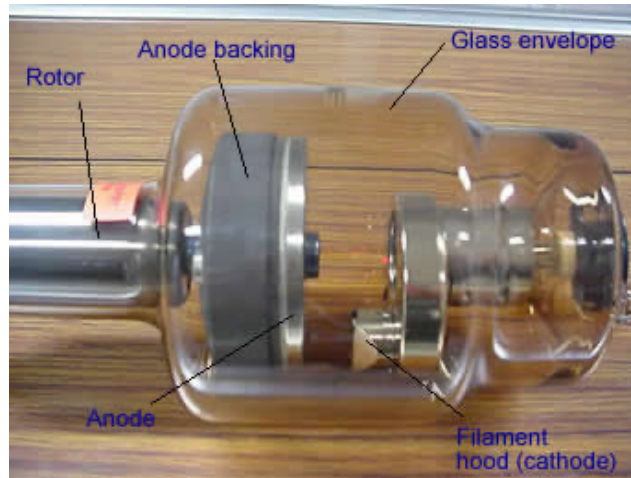
<https://radiologykey.com/projection-x-ray-imaging/>

# X-Ray Tube

- Electrons produced by heating a filament (cathode) to  $\sim 2200^{\circ}\text{C}$  - *thermionic emission*
- Electrons accelerated in an electric field (15-150 kV) and strike tungsten anode
- Electron interacting in tungsten target produces x-rays, that pass through exit window and filter
- Anode rotates



# X-Ray Tube



# X-Ray Energy

1 eV is the energy gained by an electron when it is accelerated through a potential difference of 1 V.

$$1 \text{ eV} = 1.6 \times 10^{-19} \text{ joules}$$

In an x-ray tube, if the potential applied to the tube is 50 kV (50,000V), then the maximum energy x-ray that can be produced is 50 keV

The peak voltage applied to an x-ray tube is often designated as kVp

## X-Ray Tube Current and Output

- Flow of electrons between anode and cathode represents a current
- Tube current typically 50-400 mA
- Tube output (power) = tube current x applied voltage

## Efficiency of X-Ray Production

Incident power on anode is:

$$P_i = V \times I$$

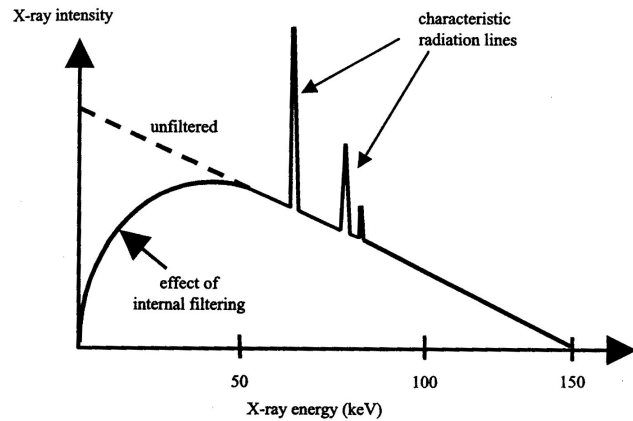
The radiated power is given by

$$P_r = 0.9 \times 10^{-9} Z V^2 I$$

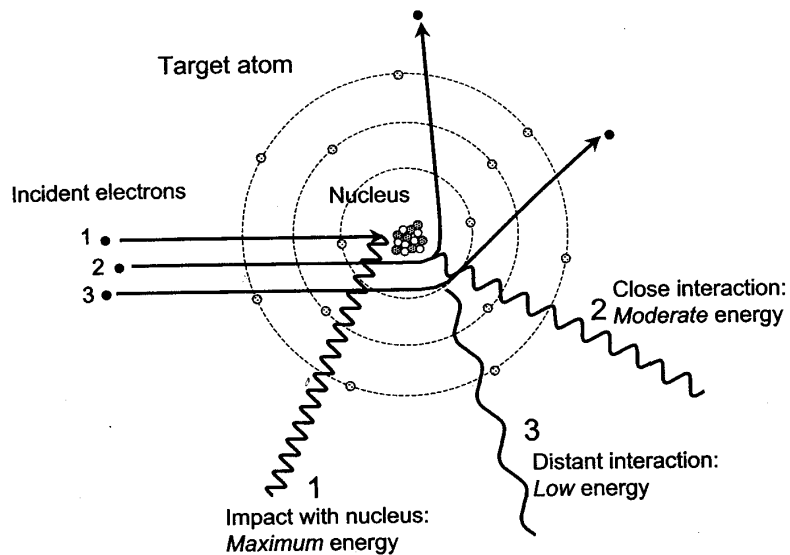
$$\text{Efficiency} = \frac{P_r}{P_i} = 0.9 \times 10^{-9} ZV \quad (\text{only } \sim 0.01\% \text{ for tungsten!})$$

# X-Ray Spectrum

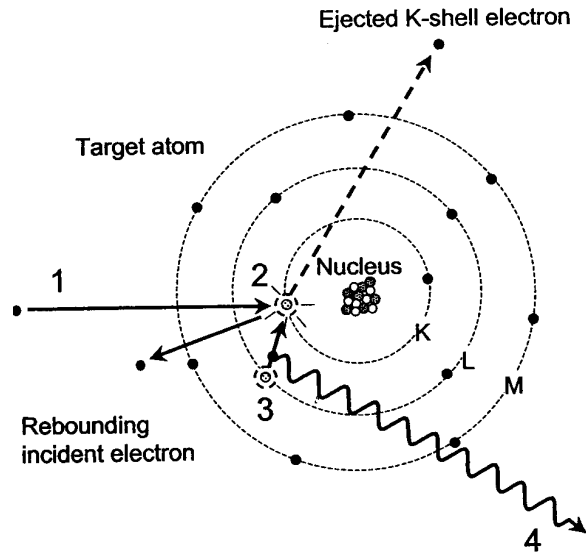
- Tube voltage = 150 kV
- Tungsten anode
- Two components
  - Continuous up to energy of 150 keV
  - Discrete lines



# Bremsstrahlung (continuous)



# Characteristic X-rays (discrete)



# Characteristic X-rays

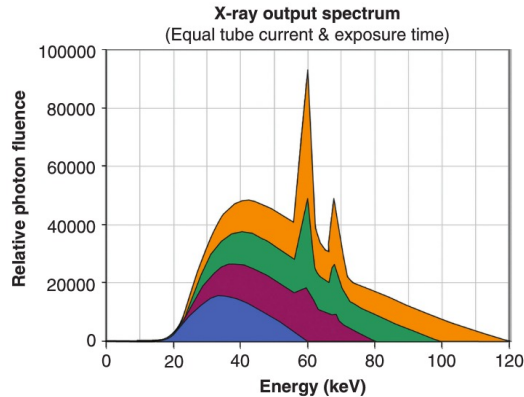
- Tungsten

**Table 3.1**  
Principal Characteristic X-Ray Energies for Tungsten

	Lines	Transition	Energy (keV)
K Series	$K\beta_2$	$N_{III} - K$	69.09
	$K\beta_1$	$M_{III} - K$	67.23
	$K\alpha_1$	$L_{III} - K$	59.31
	$K\alpha_2$	$L_{II} - K$	57.97
L Series	$L\gamma_1$	$N_{IV} - L_{II}$	11.28
	$L\beta_2$	$N_V - L_{III}$	9.96
	$L\beta_1$	$M_{IV} - L_{II}$	9.67
	$L\alpha_1$	$M_V - L_{III}$	8.40
	$L\alpha_2$	$M_{IV} - L_{II}$	8.33

Data from U.S. Department of Health, Education, and Welfare. Radiological health handbook. Rev. ed. Washington, DC: U.S. Government Printing Office, 1970.

# Effect of Tube Voltage



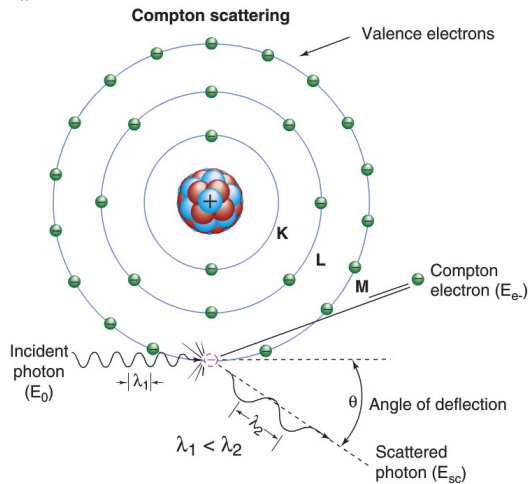
- Increases energy and number of x-rays
- Intensity proportional to square of tube voltage

# Interactions of X-Rays (and $\gamma$ rays $< 1$ MeV) with Materials

- If x-rays interact, they can be absorbed or scattered from the x-ray beam
- Two main processes occur at x-ray energies
  - Compton Scattering
  - Photoelectric Effect
  - Coherent (Rayleigh) scattering has small probability
- In tissue these create contrast necessary for imaging, but also can lead to loss of information and radiation dose
- In detectors they are the basis for detecting x-rays



# Compton Scattering



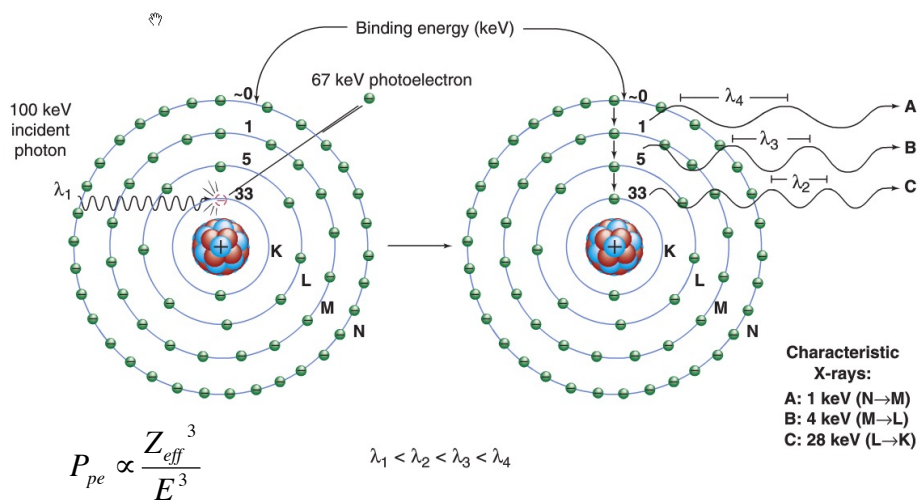
- Probability roughly proportional to material density

$$E_0 = E_{sc} + E_{e-}$$

$$E_{sc} = \frac{E_0}{1 + \frac{E_0}{mc^2} (1 - \cos\theta)}$$

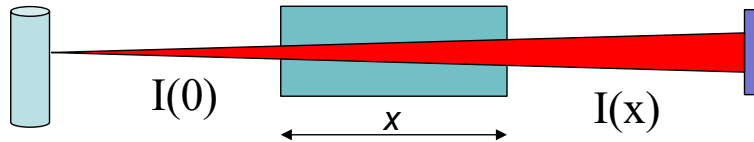
33

# Photoelectric Effect



34

## Linear Attenuation Coefficient



- If a monoenergetic x-ray beam has intensity  $I(0)$  (photons per second per  $\text{cm}^2$ ) before absorber, and intensity  $I(x)$  after passing through  $x$  cm of absorber, then the linear attenuation coefficient  $\mu$  is defined as:

$$I(x) = I(0)e^{-\mu x}$$

## Attenuation Coefficient

- Sum of individual contributions from coherent and Compton scattering, and photoelectric absorption

$$\mu = \mu_{\text{coherent}} + \mu_{\text{Compton}} + \mu_{\text{photoelectric}}$$

- Half-Value Layer (HVL)
  - Thickness of tissue that attenuates x-ray beam by one half

$$\text{HVL} = (\ln 2) / \mu$$

# HVL for Different Energies

**TABLE 1.2. The Half-Value Layer (HVL) for Muscle and Bone as a Function of the Energy of the Incident X-Rays**

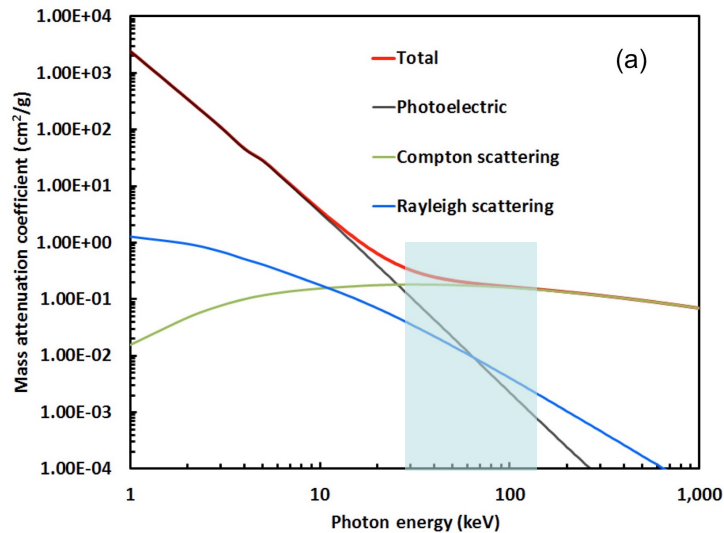
X-ray energy (keV)	HVL, muscle (cm)	HVL, bone (cm)
30	1.8	0.4
50	3.0	1.2
100	3.9	2.3
150	4.5	2.8

# Mass Attenuation Coefficient

- $\mu_m = \mu/\rho$ 
  - Units are  $\text{cm}^2/\text{g}$
  - Useful, as it normalizes for density

$$\mu_m = (\mu_{\text{coherent}} + \mu_{\text{Compton}} + \mu_{\text{photoelectric}})/\rho$$

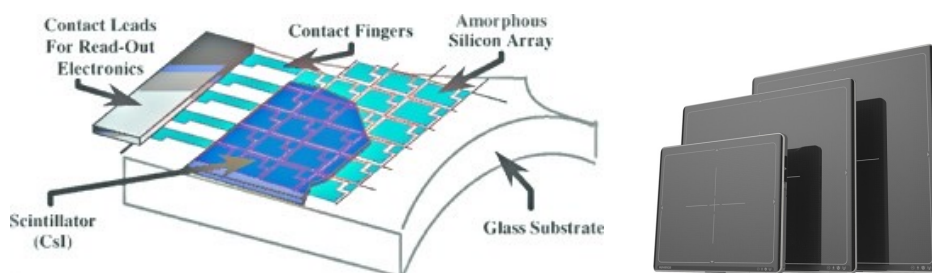
## Mass Attenuation Coefficients for Soft Tissue



Courtesy Dr. Kai Yang

39

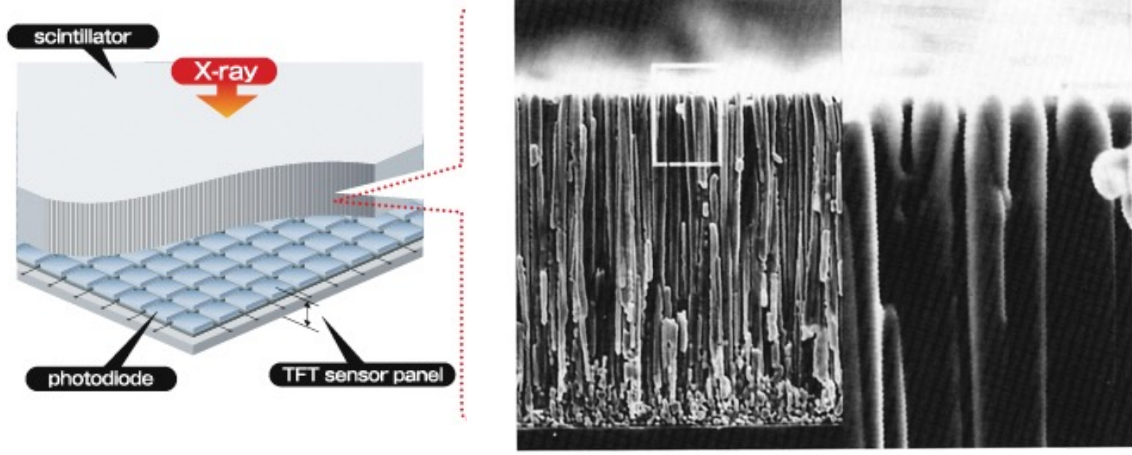
## Digital Radiography Detectors



- Large-area flat-panel detectors
- Amorphous silicon transistor array layered onto glass substrate (light detection and readout)
- CsI(Tl) scintillator deposited on top (x-ray conversion)

40

# Structured CsI(Tl) Scintillator



# Clinical X-ray Imaging System

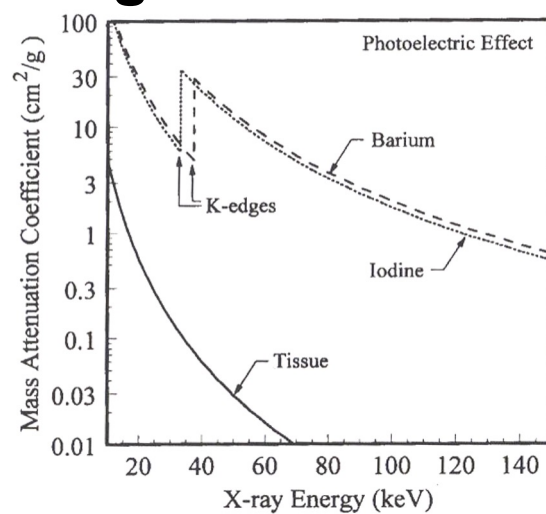


## X-Ray Contrast Agents

- Often intrinsic tissue contrast not sufficient to visualize disease
- Can introduce a “contrast agent” that increases contrast
- Contrast agent should be:
  - Non-toxic
  - Be composed of elements with an appropriate K-edge energy
    - barium (oral) and iodine (i.v.) are most common
  - Easy to administer (i.v., oral etc.)

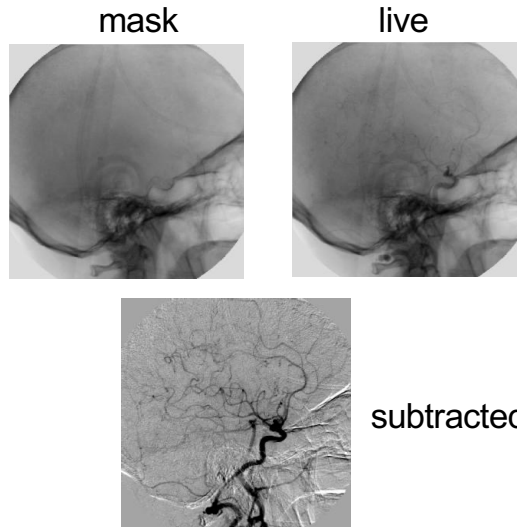
## Attenuation Coefficients for Contrast Agents

K-edge:  
Barium 37.4 keV  
Iodine 33.2 keV



# X-Ray Angiography

- Visualizes blood vessels
- Inject i-v intravascular contrast agent
- Digital subtraction angiography provides highest contrast by taking image before and after contrast agent administration
- Used for vascular problems, can resolve vessels down to 100  $\mu\text{m}$  in diameter



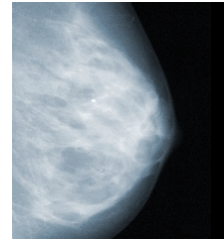
# X-Ray Fluoroscopy

- Continuous real-time imaging
- Used for placements of stents, catheters, pacemakers and other interventional surgery
- Must use low tube current to keep dose reasonable - special detection requirements



# Mammography

- Screening for breast cancer
- Breast compressed
- Magnification 1.5x to 2x
- Low energy x-rays (~ 25 -35 kVp)
- Mo anode x-ray tube (17.5 and 19.6 keV char. x-rays)
- Low dose



## Some Common Clinical Applications of Planar X-Rays

- Dental x-rays
- Mammography
- Lung disorders and diseases
- Orthopaedics
- Sports injuries and accidents
- Vascular disease (angiography)
- Image-guided interventions (fluoroscopy)



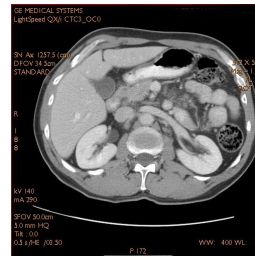
# Computed Tomography (CT)

also known as

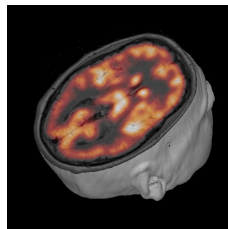
# Computed Axial Tomography (CAT)



planar x-ray



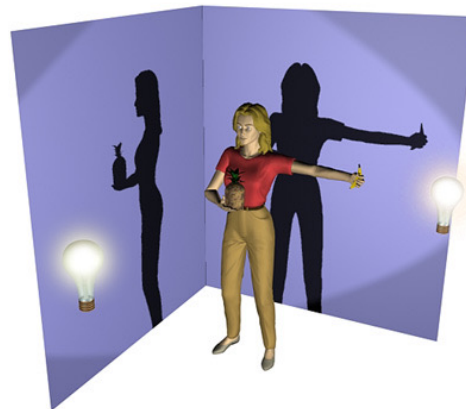
CT scan



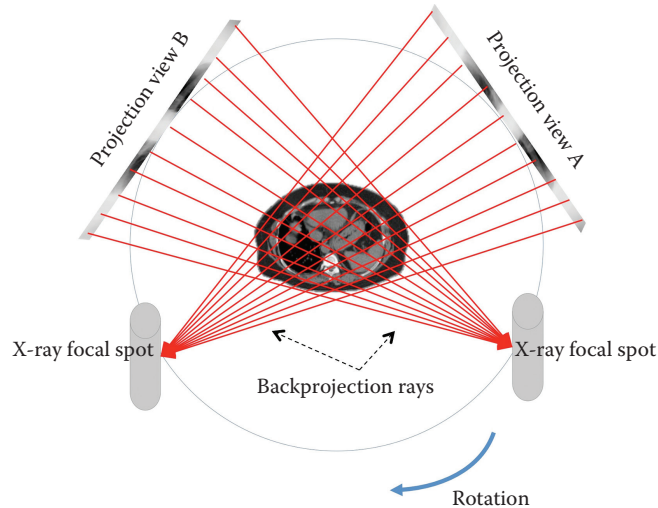
# Computed Tomography



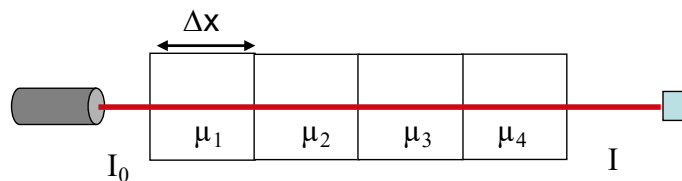
- Produces images of slices through the body
- Imaging system takes views at different angles around the patient and reconstructs the images using mathematical algorithms



# Computed Tomography (CT) Projection Views



## Converting Projection Data to be linear with $\mu$



$$I = I_0 \exp(-\mu_1 \Delta x) \times \exp(-\mu_2 \Delta x) \times \exp(-\mu_3 \Delta x) \times \exp(-\mu_4 \Delta x)$$

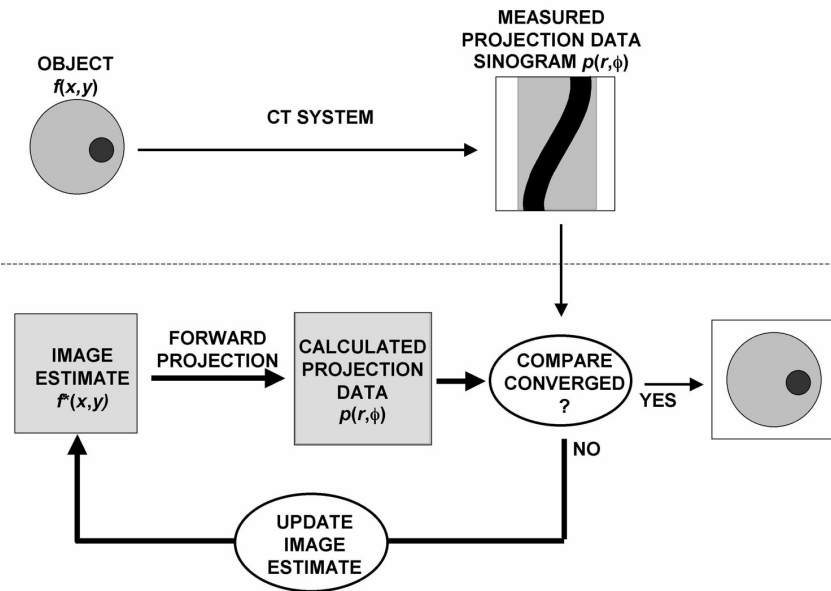
$$= I_0 \exp-(\mu_1 + \mu_2 + \mu_3 + \mu_4) \Delta x$$

$I_0$  - x-ray signal with nothing in the scanner

$$\ln \frac{I_0}{I} = (\mu_1 + \mu_2 + \mu_3 + \mu_4) \Delta x$$

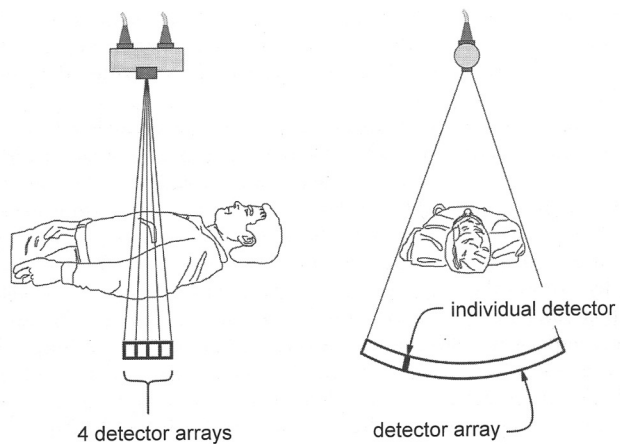
$I$  - x-ray signal measured with patient in scanner

# Iterative Reconstruction Methods



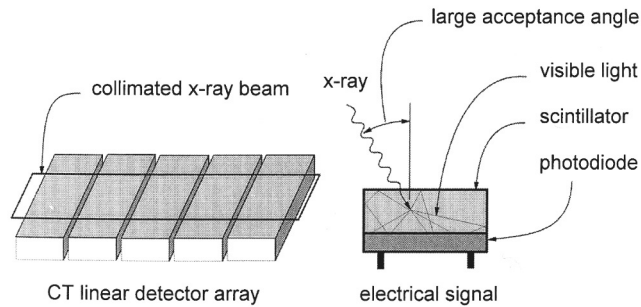
# Typical X-ray CT Scanner Multiple Detector Array

- Makes efficient use of x-ray flux by acquiring multiple slices at once



# CT Detectors

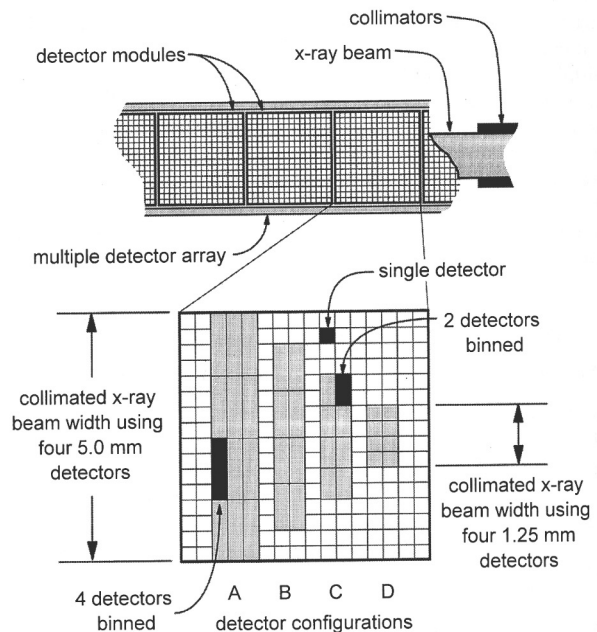
## Solid State Detectors



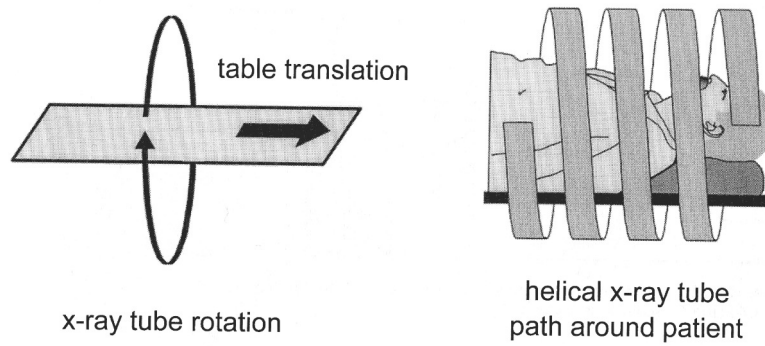
- Ceramic scintillator coupled to photodiode
- Scintillator converts x-ray to visible light
- Photodiode converts light into current

## Detector Array for CT

- Slice thickness and number of slices determined by detector binning and collimation



## Helical Scan Acquisition

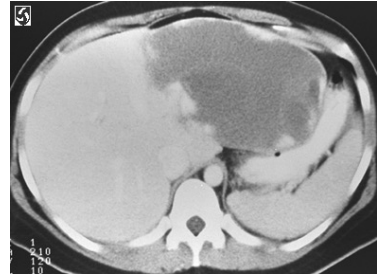
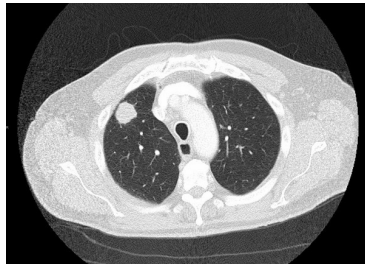


Data acquired while patient bed is moving continuously. X-ray source moves in a helical pattern about patient.

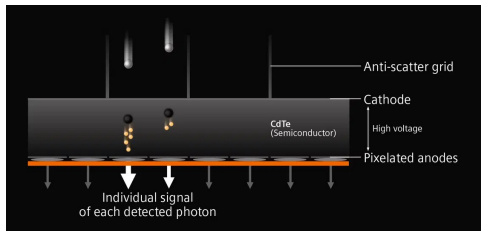
## Typical X-ray Tube Parameters for CT

- Tube potential
  - 80-140 kV
- Tube current
  - 20-500 mA
- Filtration
  - 2-3 mm Al
- Current modulation reduces x-ray flux for low attenuation regions

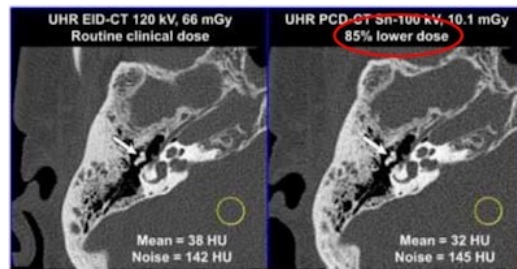
# Clinical CT scans



# Photon Counting CT



Courtesy Siemens



Courtesy Dr. Cynthia McCollough, Mayo Clinic

- Lower noise, higher contrast
- Dose reduction possible
- Higher spatial resolution
- Multispectral – material decomposition

## X-ray and $\gamma$ -ray Radiation Dose

- Absorbed dose ( $D$ ) defined as energy deposited per unit mass
  - 1 Gray (Gy) = 1 J/kg

## Effective Dose

- Attempts to factor in radiation sensitivity of different organs and type of radiation involved

$$E = \sum_T w_T \times D_T \times W_R$$

- $W_R = 1$  for x-rays and gamma rays
- Unit of  $E$  is the sievert (Sv)

# Tissue Weighting Factors

1

Tissue	$w_T$	$\Sigma w_T$
Active bone marrow, Colon, Lung, Stomach, Breast, Remainder tissues: mean equivalent dose*	0.12	0.72
Gonads	0.08	0.08
Bladder, esophagus, liver, thyroid	0.04	0.16
Endosteal tissues, brain, salivary glands, skin	0.01	0.04
<b>Total</b>		<b>1</b>

\* Remainder tissues are adrenal glands, extrathoracic airways, gallbladder, heart, kidneys, lymphatic nodes, skeletal muscle, oral mucosa, pancreas, prostate (♂), small intestine, spleen, thymus, and uterus/cervix (♀). ICRP publication 103 (2006)

## A Quick Quiz – Effective Dose










- Annual dose for US domestic pilot in 1 year
- Abdominal/pelvic CT scan
- Annual dose from natural potassium in the body
- Mammogram
- Annual natural background in Denver, CO



# Effective Dose for Diagnostic Exams

American College of Radiology  
Dose Reference Card

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	Procedure	Approximate effective radiation dose	Comparable to natural background radiation for
 <b>ABDOMINAL REGION</b>	Computed Tomography (CT) — Abdomen and Pelvis	10 mSv	3 years
	Computed Tomography (CT) — Abdomen and Pelvis, repeated with and without contrast material	20 mSv	7 years
	Computed Tomography (CT) — Colonography	6 mSv	2 years
	Intravenous Pyelogram (IVP)	3 mSv	1 year
	Radiography (X-ray) — Lower GI Tract	8 mSv	3 years
	Radiography (X-ray) — Upper GI Tract	6 mSv	2 years
 <b>BONE</b>	Radiography (X-ray) — Spine	1.5 mSv	6 months
	Radiography (X-ray) — Extremity	0.001 mSv	3 hours
 <b>CENTRAL NERVOUS SYSTEM</b>	Computed Tomography (CT) — Head	2 mSv	8 months
	Computed Tomography (CT) — Head, repeated with and without contrast material	4 mSv	16 months
	Computed Tomography (CT) — Spine	6 mSv	2 years
 <b>CHEST</b>	Computed Tomography (CT) — Chest	7 mSv	2 years
	Computed Tomography (CT) — Lung Cancer Screening	1.5 mSv	6 months
	Radiography — Chest	0.1 mSv	10 days
 <b>DENTAL</b>	Intraoral X-ray	0.005 mSv	1 day
 <b>HEART</b>	Coronary Computed Tomography Angiography (CTA)	12 mSv	4 years
	Cardiac CT for Calcium Scoring	3 mSv	1 year
 <b>MEN'S IMAGING</b>	Bone Densitometry (DEXA)	0.001 mSv	3 hours
 <b>NUCLEAR MEDICINE</b>	Positron Emission Tomography — Computed Tomography (PET/CT)	25 mSv	8 years
 <b>WOMEN'S IMAGING</b>	Bone Densitometry (DEXA)	0.001 mSv	3 hours
	Mammography	0.4 mSv	7 weeks

65

# Ultrasound

*A Brief Introduction to Medical Imaging*

Ultrasound 66

66

# Ultrasound – Basic Properties

## Advantages

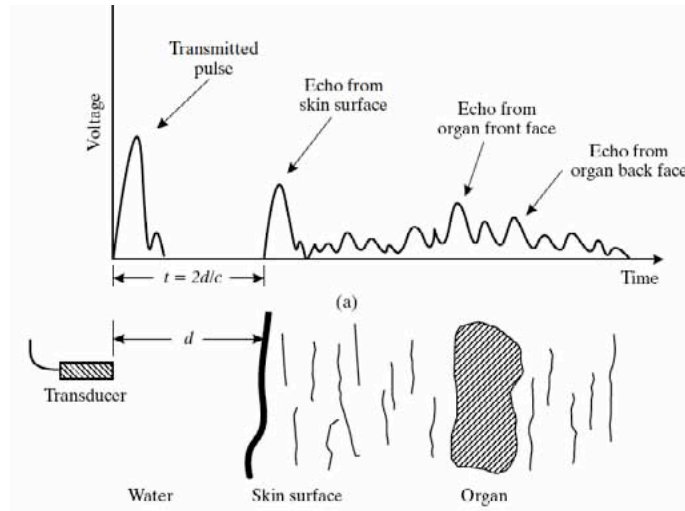
- portable
- real-time
- no ionizing radiation
- fetal imaging
- inexpensive



# Ultrasound Characteristics

- Produces images via backscattering of mechanical energy from boundaries between tissues
- Frequency: typically 1 to 10 MHz
  - Use lower frequencies for deep-lying structures
  - Higher frequencies for superficial structures
- Real-time: 30 frames/second
- Velocity = 1540 m/s in water and soft tissues
- Wavelength = 0.3 mm in water at 5 MHz

# Basic Principles of Ultrasound Imaging



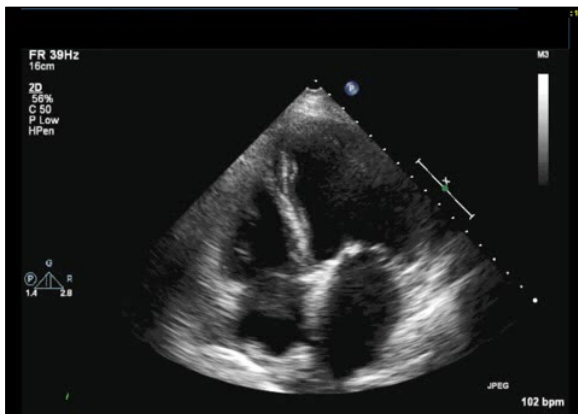
# Ultrasound Systems



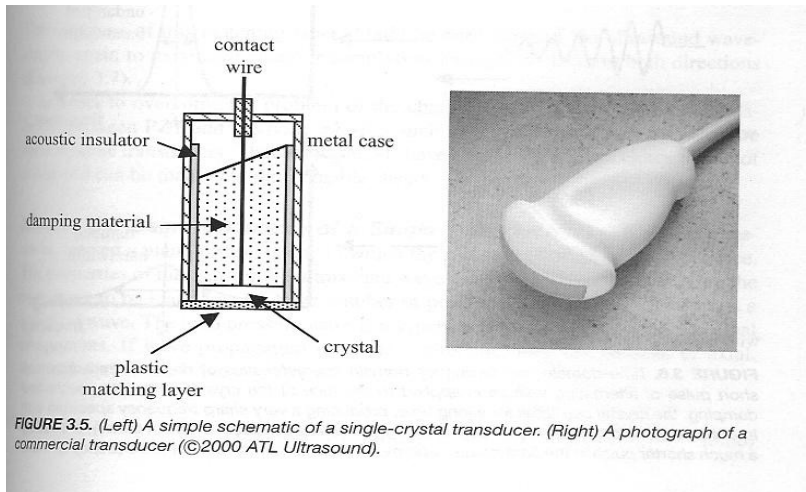
# Major Clinical Applications

- Obstetrics and gynecology
  - Fetal health
- Cardiac function
- Intra-abdominal imaging
  - Liver, kidneys, spleen and gallbladder
- Musculoskeletal applications
- Compromised flow in veins and arteries
- Tracking of needle biopsies

# Example Images



# Single Crystal Transducer



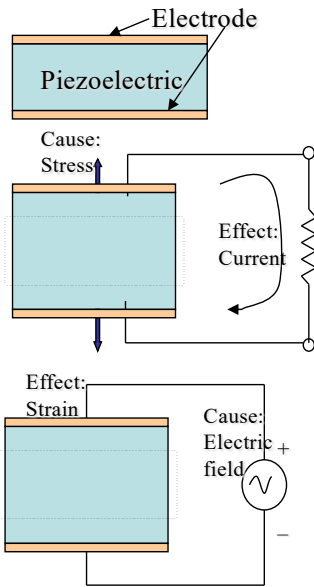
## Piezoelectric Crystal

- Commonly lead zirconate tungstate (PZT)
- Two faces of crystal coated with a thin layer of silver as electrodes
- Usually a disk which is flat or concave (for focused transducer)
- Crystal resonant frequency

$$f_0 = \frac{c_{crystal}}{2d}$$

- $c_{crystal}$  – speed of sound in crystal (~4000 m/s)
- $d$  is crystal thickness

# Piezoelectric Effect

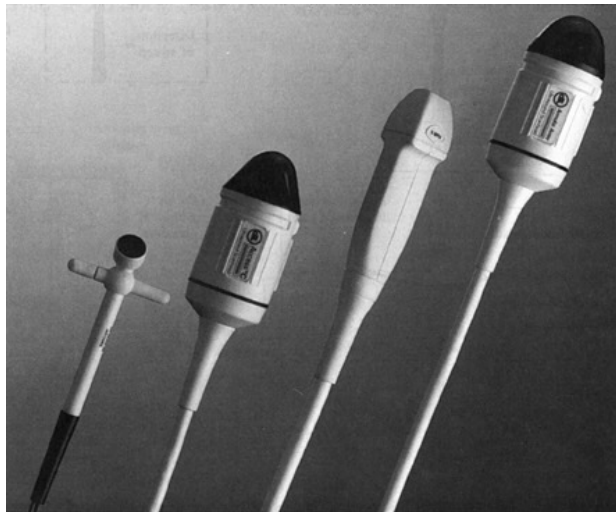


Unstrained piezoelectric material

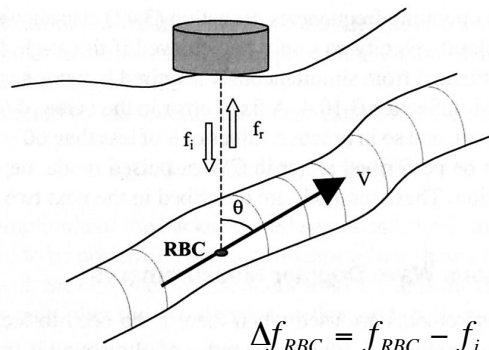
**The direct piezoelectric effect.** An applied stress results in the generation of electric charge. The charge is proportional to the stress magnitude and direction. An example is a barbecue igniter.

**The converse piezoelectric effect.** An applied electric field results in a strain. The strain is proportional to the field direction and magnitude. An example is a buzzer used in a pager.

# Ultrasonic Transducers



# Doppler Effect



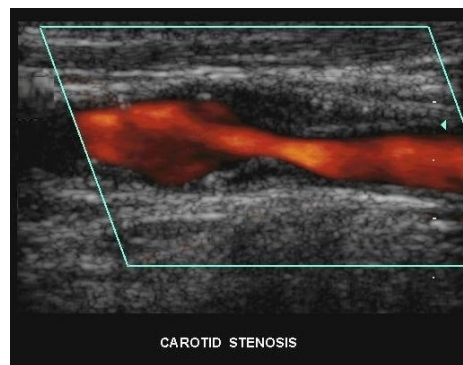
$$f_i = \frac{c}{\lambda}$$

$$f_{RBC} = \frac{c + v \cos \theta}{\lambda}$$

$$\Delta f_{RBC} = f_{RBC} - f_i = \frac{f_i v \cos \theta}{c}$$

$$\Delta f = \frac{2 f_i v \cos \theta}{c}$$

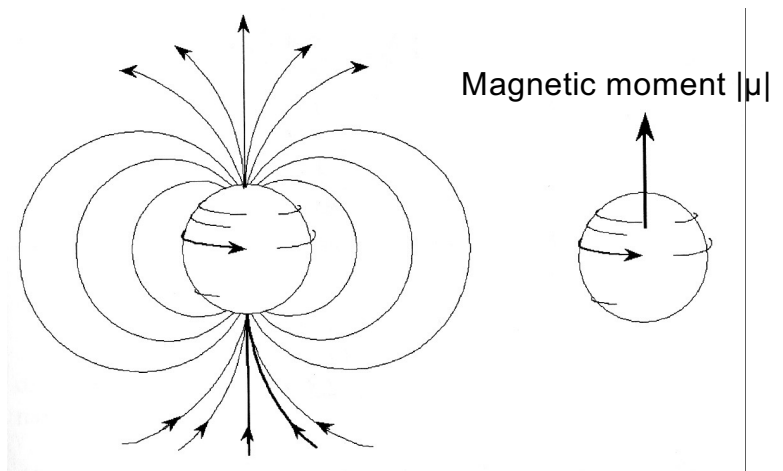
# Color Doppler Imaging



# Magnetic Resonance Imaging (MRI)

## Proton Spin and Magnetic Moment

- Protons possess a property known as spin
- Can be visualized classically as proton spinning around an axis

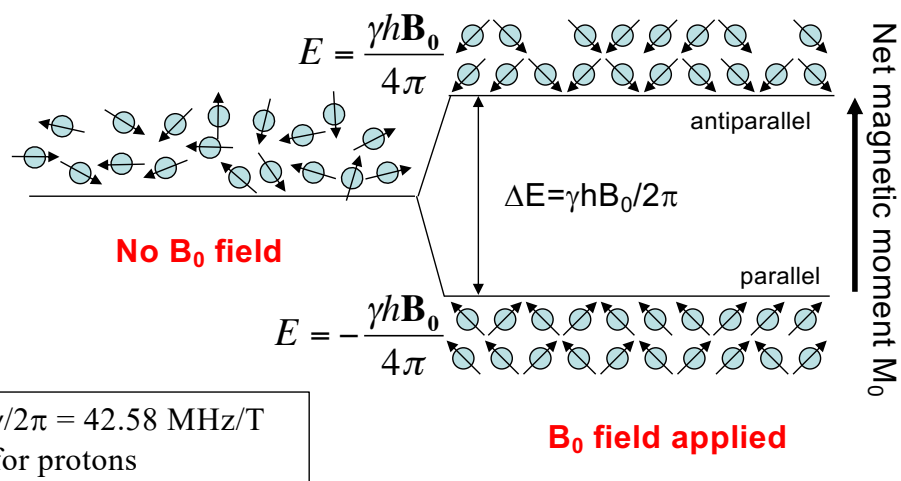




## Basic Information

- MRI primarily detects signals from protons (water, lipids)
- 1 liter water  $\sim 3 \times 10^{26}$  protons
- Human body: 70% is water
- 1 Tesla = 10,000 Gauss
- MRI magnet strengths, 0.2 T up to 11 T
- Earth's magnetic field: 50  $\mu$ T
- Can explain MRI using two approaches
  - Quantum mechanical description
  - Classical description

## Ensemble of Protons in a Magnetic Field



## Some Numbers

Compute  $\Delta E$  (assume protons and  $B_0=1.5\text{T}$ )

$$\Delta E = \frac{\gamma h B_0}{2\pi} = (42.58 \times 10^6) \times 1.5 \times (6.63 \times 10^{-34}) = 4.2 \times 10^{-26} \text{ J}$$

Where is this in electromagnetic spectrum?

$$f = \frac{E}{h} = \frac{\gamma B_0}{2\pi} = (42.58 \times 10^6) \times 1.5 = 63.9 \text{ MHz}$$

$f$  is called the Larmor frequency

## Population of Energy Levels

$$\frac{N_{\text{antiparallel}}}{N_{\text{parallel}}} = \exp\left(-\frac{\Delta E}{kT}\right) = \exp\left(-\frac{\gamma h B_0}{2\pi kT}\right)$$

$T$  = temperature (K)

$k$  = Boltzmann constant  $1.38 \times 10^{-23} \text{ J/K}$

$h$  = Planck's constant  $6.63 \times 10^{-34} \text{ Js}$

$\Delta E$  = difference in energy levels

## Some More Numbers...

What is relative population of two energy levels for protons at 1.5T and at room temperature?

$$\frac{N_{\text{antiparallel}}}{N_{\text{parallel}}} = \exp\left(-\frac{\Delta E}{kT}\right) = \exp\left(-\frac{\gamma h B_0}{2\pi kT}\right) = 0.999990$$

So only ten parts in a million difference between population of two energy states.

But 1 mm<sup>3</sup> (1 μL) of tissue contains ~ 3 x 10<sup>20</sup> protons, so this are still 3 x 10<sup>15</sup> protons more in lower energy state than higher energy state.

## Larmor Frequency

The Larmor precession frequency  $f_0$  is the frequency of the electromagnetic field that must be applied for transitions to occur between the parallel and antiparallel energy levels

$$\Delta E = \frac{\gamma h B_0}{2\pi}$$

$$f_0 = \frac{\gamma B_0}{2\pi}$$

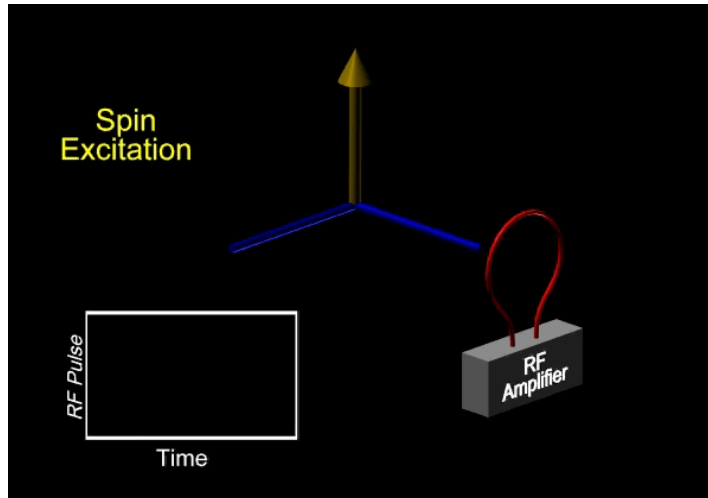
## How is the signal in MRI obtained?

- Need to produce changing magnetic field. This can induce a current in a coil (so far net magnetic moment is stationary)
- To do this, we can “tip” some magnetization into the x-y plane
- Accomplished by using a second magnetic field orthogonal to  $B_0$  with a frequency given by the Larmor frequency

## Application of $B_1$ Field

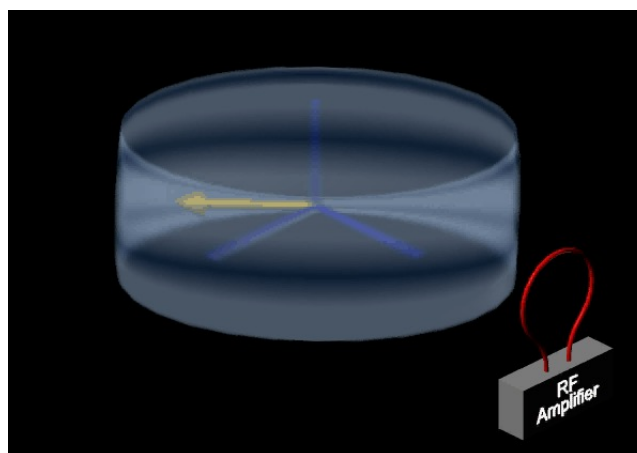
- In MRI, an additional magnetic field, called the  $B_1$  field is applied
- This field is applied in the transverse x-y plane
- It is a time-varying field with a frequency equal to the Larmor frequency  $f_0$
- This can excite spins from parallel to anti-parallel orientation, changing the magnitude of  $M_z$

# Creating the Signal



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# Detecting the Signal

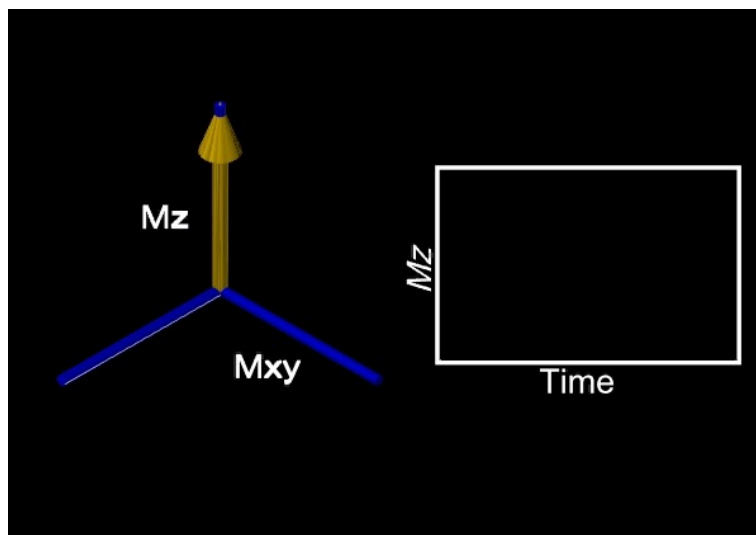


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## Signal Decay

- After application of pulse, MRI signal does not stay constant, but actually decays away.
- RF pulse transfers energy from coil to protons, resulting in non-Boltzmann distribution of population of states
- Each of the components of magnetization will return to their equilibrium values over time

## $T_1$ and $T_2$ Relaxation



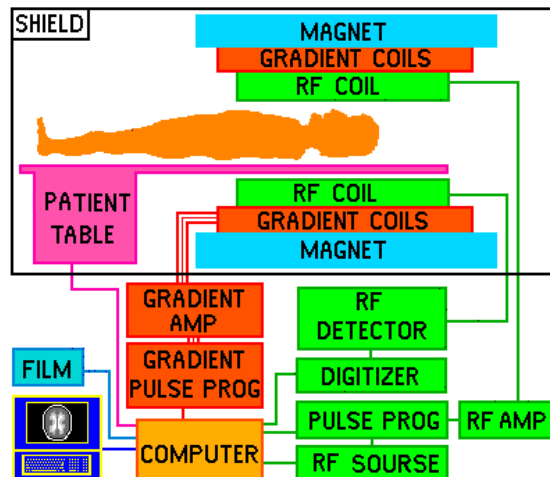
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# Tissue $T_1$ and $T_2$ values

**TABLE 4.2. Tissue Relaxation Times at 1.5 T**

Tissue	$T_1$ (ms)	$T_2$ (ms)
Fat	260	80
Muscle	870	45
Brain (gray matter)	900	100
Brain (white matter)	780	90
Liver	500	40
Cerebrospinal fluid	2400	160

# Components of MRI Scanner



# Magnets

- **Permanent Magnet**
  - For fields up to ~ 0.35 Tesla
  - Relatively low cost, no cooling required, limited stray field
  - Open systems can be designed (patient is in-between the two poles)
  - **Problem:** field homogeneity and stability depends on room-temperature
- **Resistive Magnets**
  - For fields up to ~ 0.35 Tesla
  - Constant current ( $i$ ) through a conductor  $B_0 \sim i$
  - Resistance of conductor causes heat
  - **Problem:** field homogeneity and stability depends on room-temperature
- **Superconducting Magnets**
  - At very low temperatures, resistance of conductor  $\rightarrow$  zero!
  - Works usually without power consumption (once the current has been fed in, it runs forever if the temperature is low enough ( $<10$  K).
  - Superconducting coil (special alloy) is embedded in liquid nitrogen, vacuum, and helium.
  - Shim coils are used to fine-tune the field homogeneity.

# Gradient Coils

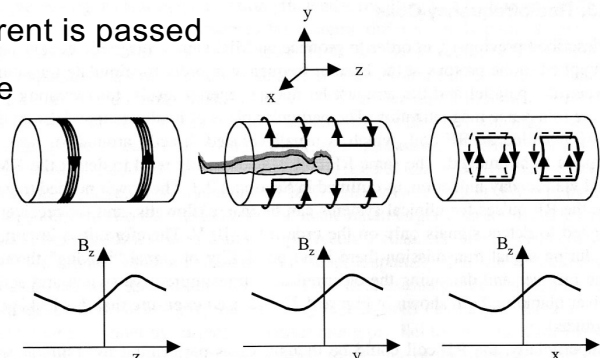
Used to alter Larmor frequency vary as a function of location  $\rightarrow$  imaging

Field strength small compared with main field ( $\sim 20\text{-}40$  mT/cm)

Can use conventional conductors (copper) at room temperature (water cooled for heat dissipation)

Consist of loops of wire through which current is passed

Cylindrical geometry to match magnet bore





# RF-Coils



Head RF-coil  
(volume coil)

# Instrumentation Clinical MRI Scanner

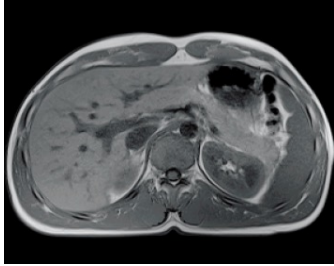


Low-field system 0.35 T (Siemens)

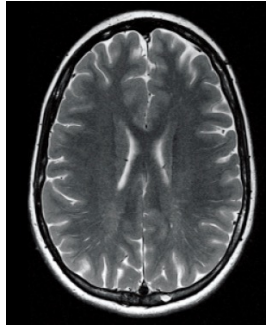


Avanto 1.5 T (Siemens)

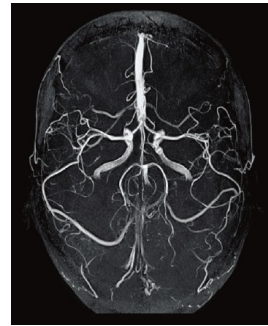
# 1.5 T Clinical MRI Images



T1 weighted  
Multi breath-holding  
1.5 T Magnetom Avanto



T2 weighted  
1.5 T Magnetom Avanto



T2 weighted Angio  
1.5 T Magnetom Avanto